

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: 93117408.0

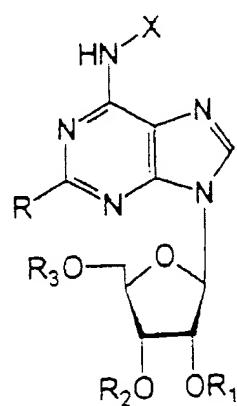
(51) Int. Cl.⁵: A61K 31/70, C07H 19/16

(22) Date of filing: 27.10.93

(30) Priority: 27.10.92 JP 312764/92
 27.10.92 JP 312765/921-2, Hiranomachi Nichome
 Chuo-ku, Osaka (JP)(43) Date of publication of application:
 15.06.94 Bulletin 94/24(72) Inventor: Yamada, Toshio, c/o Inst. of
 Bio-Active Science
 Nippon Zoki Pharma. Co.,Ltd.,
 442-1, Kinashi
 Yashiro-cho, Katoh-gun, Hyogo (JP)(54) Designated Contracting States:
 AT BE CH DE DK ES FR GB GR IE IT LI LU MC
 NL PT SE(58) Date of deferred publication of the search report:
 12.10.94 Bulletin 94/41(74) Representative: Hansen, Bernd, Dr.
 Dipl.-Chem. et al
 Hoffmann, Eitle & Partner,
 Patentanwälte,
 Arabellastrasse 4
 D-81925 München (DE)(71) Applicant: NIPPON ZOKI PHARMACEUTICAL
 CO., LTD.

(52) Adenosine deaminase inhibitor.

(57) The use of a compound represented by the following general formula (I) or a pharmaceutically acceptable salt thereof



(I)

wherein each of R₁, R₂ and R₃ which may be same or different is hydrogen or alkyl; and R and X have the meanings given in the specification, for the preparation of a medicament which is an adenosine deaminase inhibitor is disclosed. Some of the compounds of formula (I) are novel compounds. They may be used for the making of a medicament which is for the prevention or therapy of ischemic heart diseases, diseases caused by cerebrovascular disorders, renal diseases and allergic diseases and of post-operative complicated diseases involved with activated oxygen which is generated in ischemic areas during the recirculation of blood after operations.



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 93 11 7408

DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)		
X	EP-A-0 269 574 (NIPPON ZOKI PHARMACEUTICAL CO., LTD.) * page 3, line 31 - page 4, line 29; examples 1, and, 2 * ---	1-14	A61K31/70 C07H19/16		
X	BIOCHEMICAL PHARMACOLOGY, vol.41, no.11, 1991, NEW YORK pages 1615 - 1624 J.G.NIEDZWICKI ET AL. 'Structure-Activity Relationship of Ligands of Human Plasma Adenosine Deaminase2.' * abstract * * page 1619, line 15; example LXXXII * ---	1-14			
Y	WO-A-92 05177 (RHONE-POULENC RORER INTERNATIONAL) * claim 1 * ---	1-14			
X	EP-A-0 490 818 (SANDOZ-PATENT-GMBH) * abstract * ---	1-14			
Y	EP-A-0 378 518 (NIPPON ZOKI PHARMACEUTICAL CO., LTD.) * abstract * ---	1-14	A61K C07H		
Y	WO-A-88 03147 (WARNER-LAMBERT COMPANY) * abstract * ---	1-14			
Y	EP-A-0 181 129 (WARNER-LAMBERT COMPANY) * abstract * ---	1-14			
Y	EP-A-0 219 876 (YAMASA SHPYU K.K.) * abstract * ---	1-14			
		-/-			
The present search report has been drawn up for all claims					
Place of search	Date of completion of the search	Examiner			
THE HAGUE	3 August 1994	Scott, J			
CATEGORY OF CITED DOCUMENTS					
X : particularly relevant if taken alone	T : theory or principle underlying the invention				
Y : particularly relevant if combined with another document of the same category	E : earlier patent document, but published on, or after the filing date				
A : technological background	D : document cited in the application				
O : non-written disclosure	I : document cited for other reasons				
P : intermediate document	& : member of the same patent family, corresponding document				



Europäisches
Patentamt

GEBÜHRENPFlichtIGE PATENTANSPRÜCHE

Die vorliegende europäische Patentanmeldung enthielt bei ihrer Einreichung mehr als zehn Patentansprüche.

- Alle Anspruchsgebühren wurden innerhalb der vorgeschriebenen Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für alle Patentansprüche erstellt.
- Nur ein Teil der Anspruchsgebühren wurde innerhalb der vorgeschriebenen Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für die ersten zehn sowie für jene Patentansprüche erstellt für die Anspruchsgebühren entrichtet wurden.
nämlich Patentansprüche:
- Keine der Anspruchsgebühren wurde innerhalb der vorgeschriebenen Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für die ersten zehn Patentansprüche erstellt.

MANGELNDE EINHEITLICHKEIT DER ERFINDUNG

Nach Auffassung der Rechernenzulassung entspricht die vorliegende europäische Patentanmeldung nicht den Anforderungen an die Einheitlichkeit der Erfindung; sie enthält mehrere Erfindungen oder Gruppen von Erfindungen,
nämlich:

1. Patentansprüche 1-3, 5-35: Bandage mit Pelotte (50) sowie Bandage mit Pelotte (150).
2. Patentanspruch 4: Bandage mit Pelotte (60, 60').

- Alle weiteren Recherchengebühren wurden innerhalb der gesetzten Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für alle Patentansprüche erstellt.
- Nur ein Teil der weiteren Recherchengebühren wurde innerhalb der gesetzten Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für die Teile der Anmeldung erstellt, die sich auf Erfindungen beziehen, für die Recherchengebühren entrichtet worden sind.
nämlich Patentansprüche:
- Keine der weiteren Recherchengebühren wurde innerhalb der gesetzten Frist entrichtet. Der vorliegende europäische Recherchenbericht wurde für die Teile der Anmeldung erstellt, die sich auf die zuerst in den Patentansprüchen erwähnte Erfindung beziehen.
nämlich Patentansprüche: - 3, 5-35



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 93 11 7408

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
Y	<p>BIOCHEMISTRY, vol.15, no.13, 1976 pages 2735 - 2740</p> <p>Z.KAZIMIERCZUK ET AL. 'Methylation of Adenosine in Strongly Alkaline Medium: Preparation and Properties of O'-Methyl Derivatives of Adenosine and N6-Methyladenosine.'</p> <p>* the whole document *</p> <p>---</p>	1-14	
Y	<p>NUCLEOSIDES AND NUCLEOTIDES, vol.10, no.8, 1991 pages 1677 - 1692</p> <p>G.MAURY ET AL. 'Inhibition and Substrate Specificity of Adenosine Deaminase. 2',3'- and/or 5'-Substituted Adenine Nucleoside Derivatives.'</p> <p>* the whole document *</p> <p>-----</p>	1-14	
			TECHNICAL FIELDS SEARCHED (Int.Cl.5)
<p>The present search report has been drawn up for all claims</p>			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	3 August 1994	Scott, J	
CATEGORY OF CITED DOCUMENTS		<p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>	
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p>			



LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims : 1-3,9-14 in part :

The use of compounds of formula (I)
claim 1, where R1=alkyl, R2=H, R3=H,
R=H and X=H as adenosine deaminase
inhibitors, pharmaceutical
compositions containing them, their
use, and medicaments containing them.

2. Claims : 1,2,4,5,9-14 in part ; 8 wholly :

The use of compounds of formula (I)
claim 1, where R1=alkyl, R2=H, R3=H,
R=H and X is other than H as adenosine
deaminase inhibitors, compounds of
formula (Ia), claim 5, pharmaceutical
compositions containing them, their
use, and medicaments containing them.

3. Claims : 1-7,9-14 in part :

The use of compounds of formula (I)
claim 1, where R1=alkyl, R2=H, R3=H,
and R is other than H as adenosine
deaminase inhibitors, compounds of
formula (Ia), claim 5; (Ib), claim 6;
(Ic), claim 7, pharmaceutical
compositions containing them, their
use, and medicaments containing them.

4. Claims : 1-7,9-14 in part :

The use of compounds of formula (I),
claim 1, where two or three of R1,R2,
R3 are alkyl as adenosine deaminase
inhibitors, compounds of formula (Ia),



European Patent
Office

EP 93 11 7408 -B2-

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

claim 5; (Ib), claim 6; (Ic), claim 7, pharmaceutical compositions containing them, their use, and medicaments containing them.

5. Claims : 1,9-14 in part :

The use of compounds of formula (I), claim 1, where R1=H, R2=H, R3=alkyl as adenosine deaminase inhibitors pharmaceutical compositions containing them, their use, and medicaments containing them.

6. Claims : 1-7,9-14 in part :

The use of compounds of formula (I), claim 1, where R1=H, R2=alkyl, R3=H as adenosine deaminase inhibitors, compounds of formula (Ia), claim 5; (Ib), claim 6; (Ic), claim 7, pharmaceutical compositions containing them, their use, and medicaments containing them.

The subject-matter searched and proposed for search defines solely the scope of the subject for the purpose of search and may not as defined satisfy the requirement of Article 123(2), EPC, with regard to possible granting of such subject-matter.

Since only the first subject-matter has been searched, then the search division reserves the right to formulate further non-unities should the necessity arise.